Berlex Laboratories

Protocol 305602:

A Multinational, Multicenter, Randomized, Double-Blind, Placebo Controlled, Dose-Response Study to Evaluate the Efficacy and Safety of Ad5FGF-4 in Patients with Stable Angina

NON-TECHNICAL ABSTRACT

This is a clinical research study with a gene therapy treatment known as Ad5FGF-4. The purpose of the study is to see if this new gene therapy can help produce the growth of blood vessels in the heart, thus reducing the frequency and severity of angina. Angina is a disease that causes pain in the chest when the body demands more blood than the heart can supply, normally during exercise. New blood vessels would supply more oxygen to the heart, and therefore reduce chest pain.

The study will be carried out in hospitals around the world and at least 450 suitable patients aged 30 to 75 will be recruited. Suitable patients will be those who have a history of stable angina and who, despite medication, are still experiencing angina pains. Patients will receive either the active drug (Ad5FGF-4) (one of two possible doses) or a placebo; approximately 2/3 of patients will receive active drug and approximately 1/3 will receive placebo.

The study drug, Ad5FGF-4, is an experimental gene therapy treatment in the early stages of development. Gene therapy is a new form of treatment in which genes are introduced into cells. Genes occur naturally in all cells of the body and are the building blocks that determine physical characteristics.

The study drug is made up of two parts – an active gene therapy and a carrier. The gene used in this treatment is the FGF-4 gene; this causes the production of a protein known as **F**ibroblast **G**rowth **F**actor **4**. FGF-4 has been found to make blood vessels grow in animals.

The gene (FGF-4) is carried into the heart by a modified (changed) adenovirus. This type of virus is usually associated with the common cold but in this study the adenovirus has been changed so it cannot multiply and cause symptoms.

Patients participating in this study are required to undergo the following:

Baseline period: a general health screening; an evaluation of heart activity; questionnaires and a diary about how the patient copes with exercise and the quality of life; and an exercise treadmill test.

In hospital period: An overnight hospital stay including cardiac (heart) catheterization; coronary angiography; and study medication administration.

Short-term Follow-up: Blood, urine, stool, and throat swabs will be collected; physical examinations and an ECG will be performed, and diaries will be completed. At weeks 4 and 12 the exercise treadmill test will be repeated.

Long-term Follow-up (months 6, 12, 18, 2, 36, 48, 60): full physical examinations, ECG (month 6 and 12 only), blood, urine and stool sample collection; exercise treadmill test (month 6 only).

When the month 60 (5 years) visit has been completed, the patients will be contacted only yearly for the next 10 years, by postcard, to complete a short health questionnaire.

The efficacy of the study drug will be evaluated by examination of data from the exercise treadmill tests and quality of life questionnaires. Dose response will also be examined based on the two doses of study drug used. Short-term, medium-term, and long-term safety data will be analyzed.